
Long-Term Health Effects of Embedded Depleted Uranium

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The Embedded Pellet Rat Model

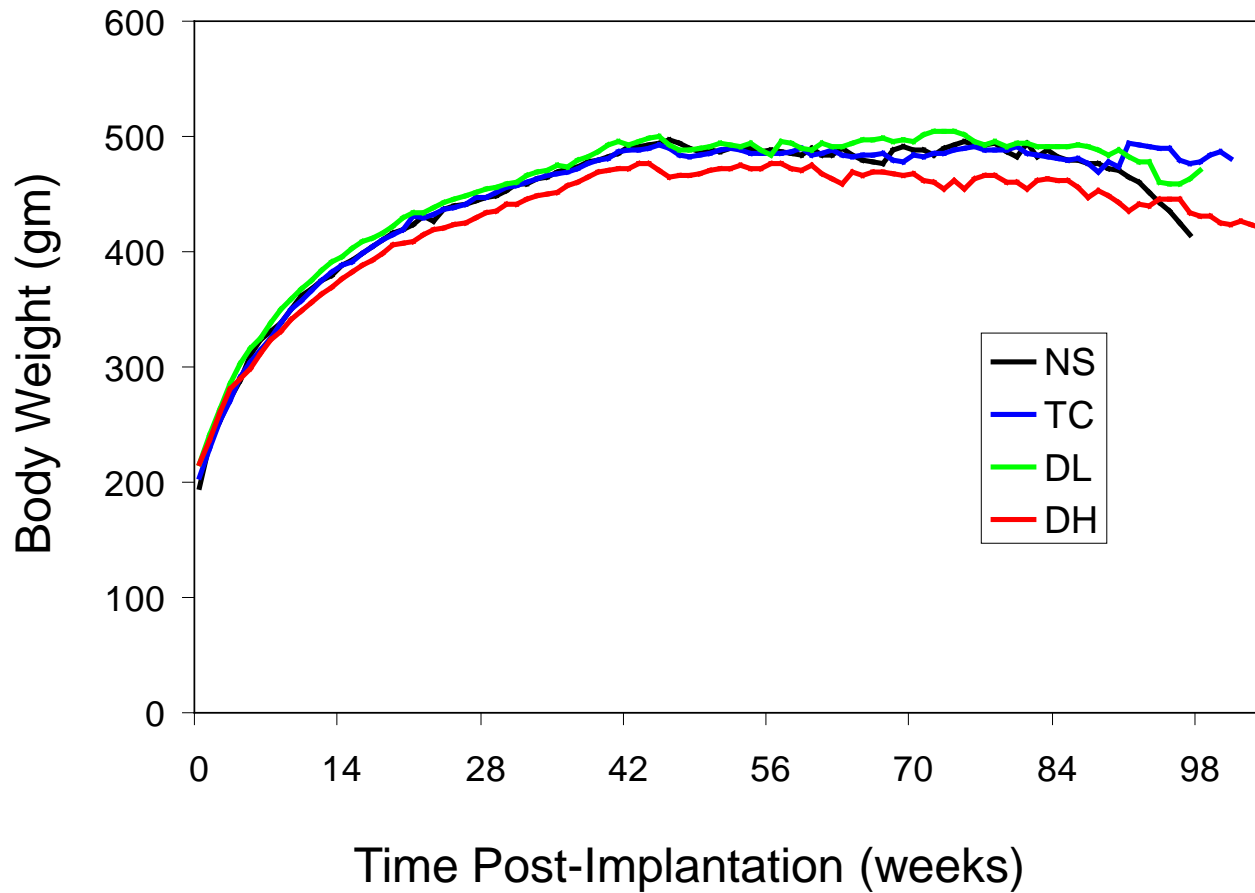


X-ray of pellets implanted in gastrocnemius muscle

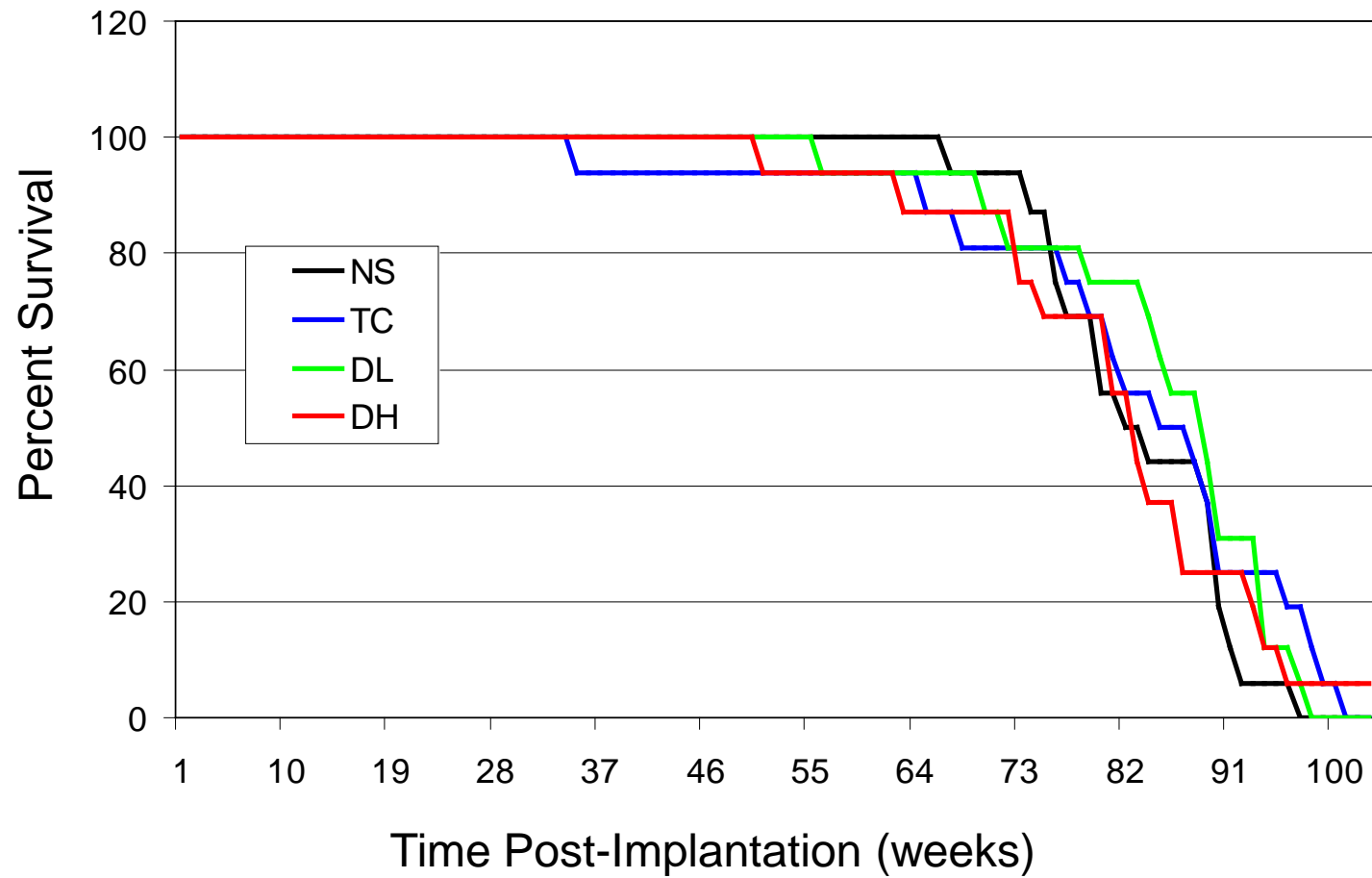
Experimental Approach

- Two-year longevity study to determine whether intramuscularly implanted DU or tungsten alloy pellets are carcinogenic.
- Six treatment groups of Fisher 344 rats
 - **Two groups with 4 or 20 DU pellets**
 - Two groups with 4 or 20 tungsten alloy pellets (91% W, 6% Ni, 3% Co)
 - One nickel group (positive control)
 - One tantalum group (negative control)
- One set of pellet-implanted rats for duration of study. Second set includes rats euthanized at selected times after pellet implantation to provide tissues for histopathology, assessment for metal content and immunotoxicity testing.
- USAMRMC Award DAMD17-01-1-0821

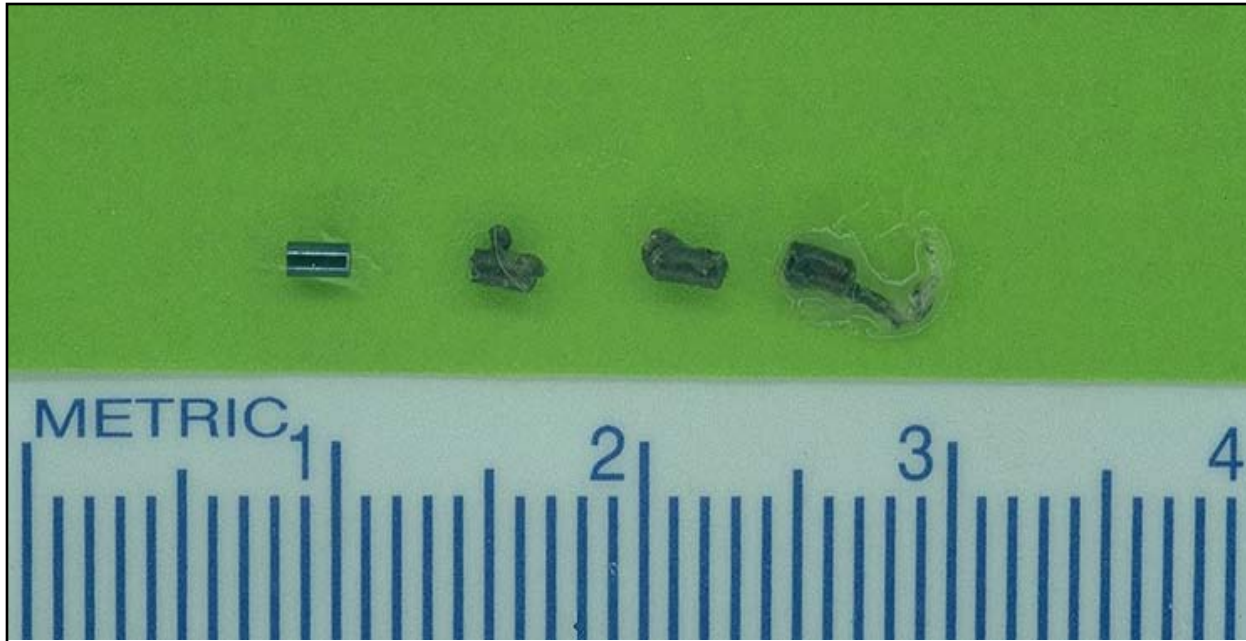
Body Weight Gain After Pellet Implantation



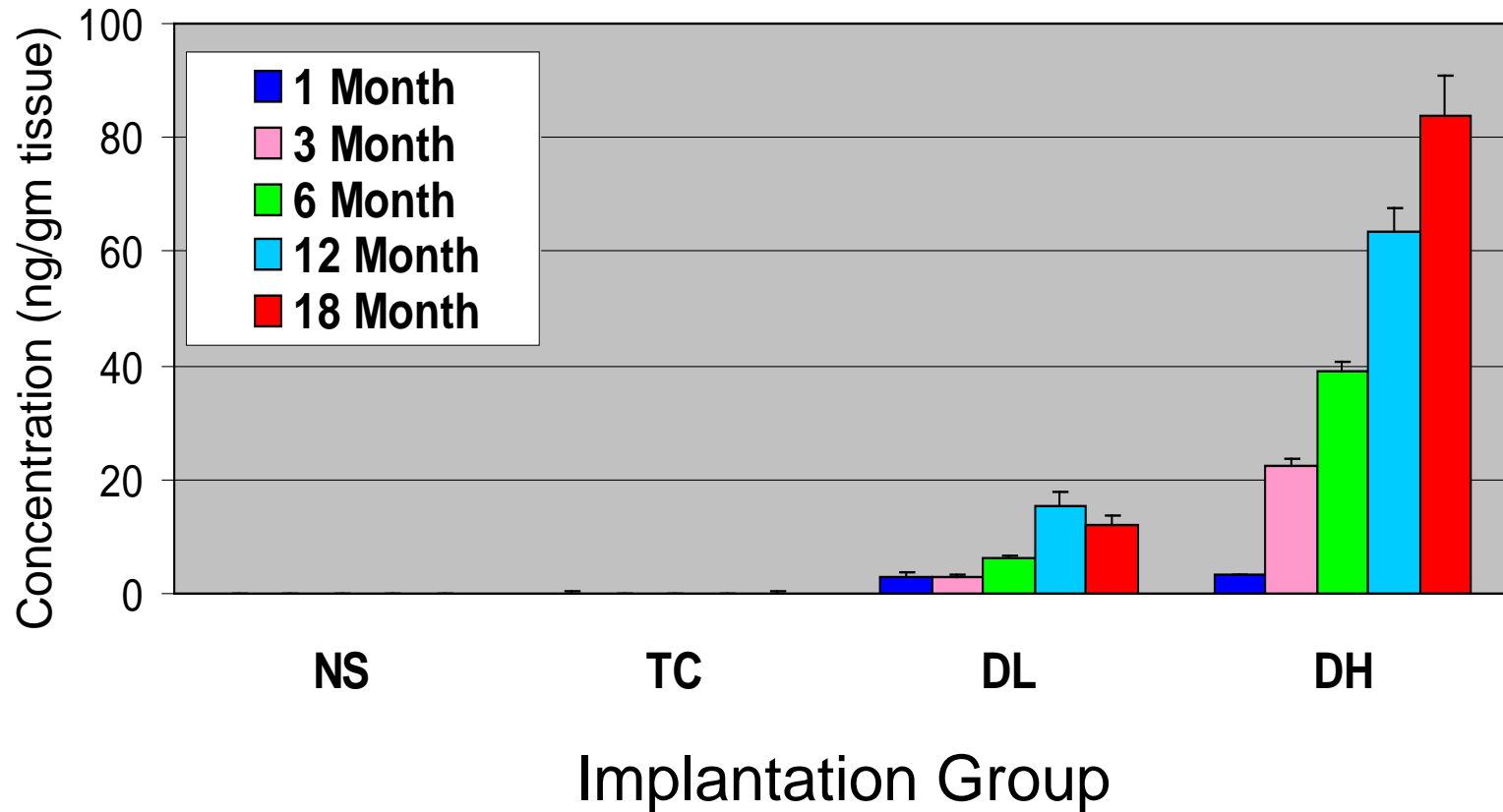
Survival After Pellet Implantation



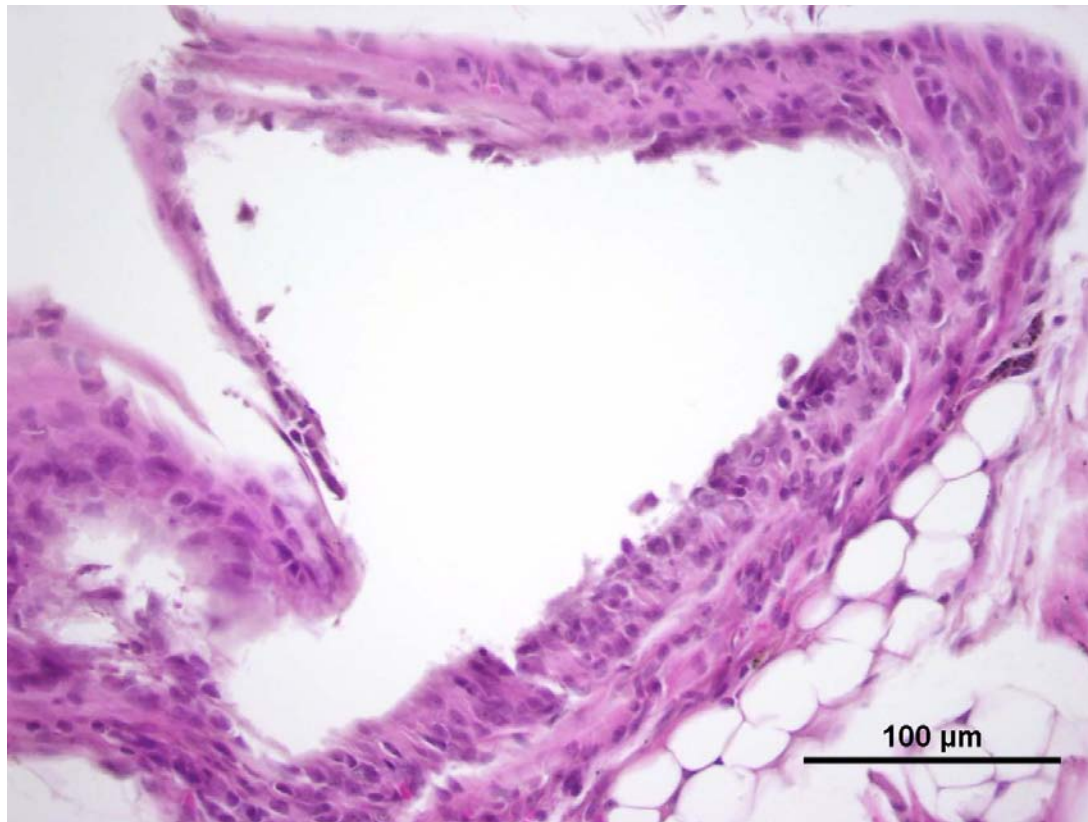
DU pellet implants: new and 12 weeks



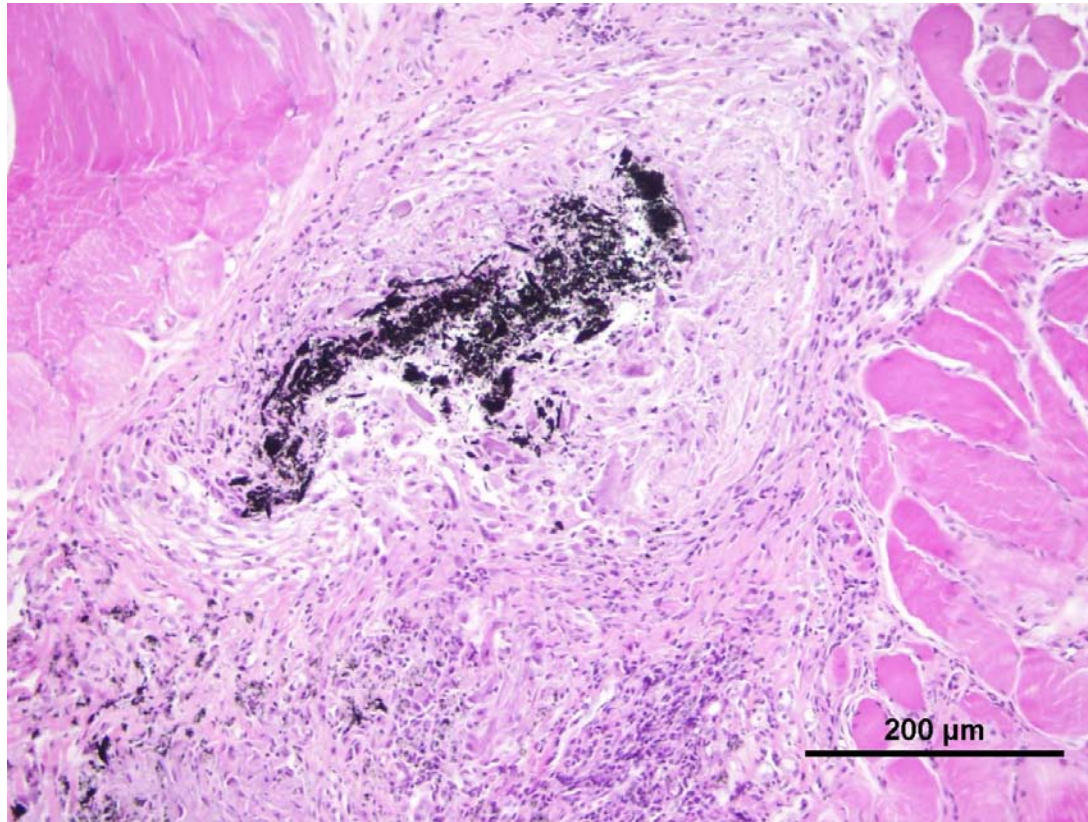
Spleen Uranium Levels



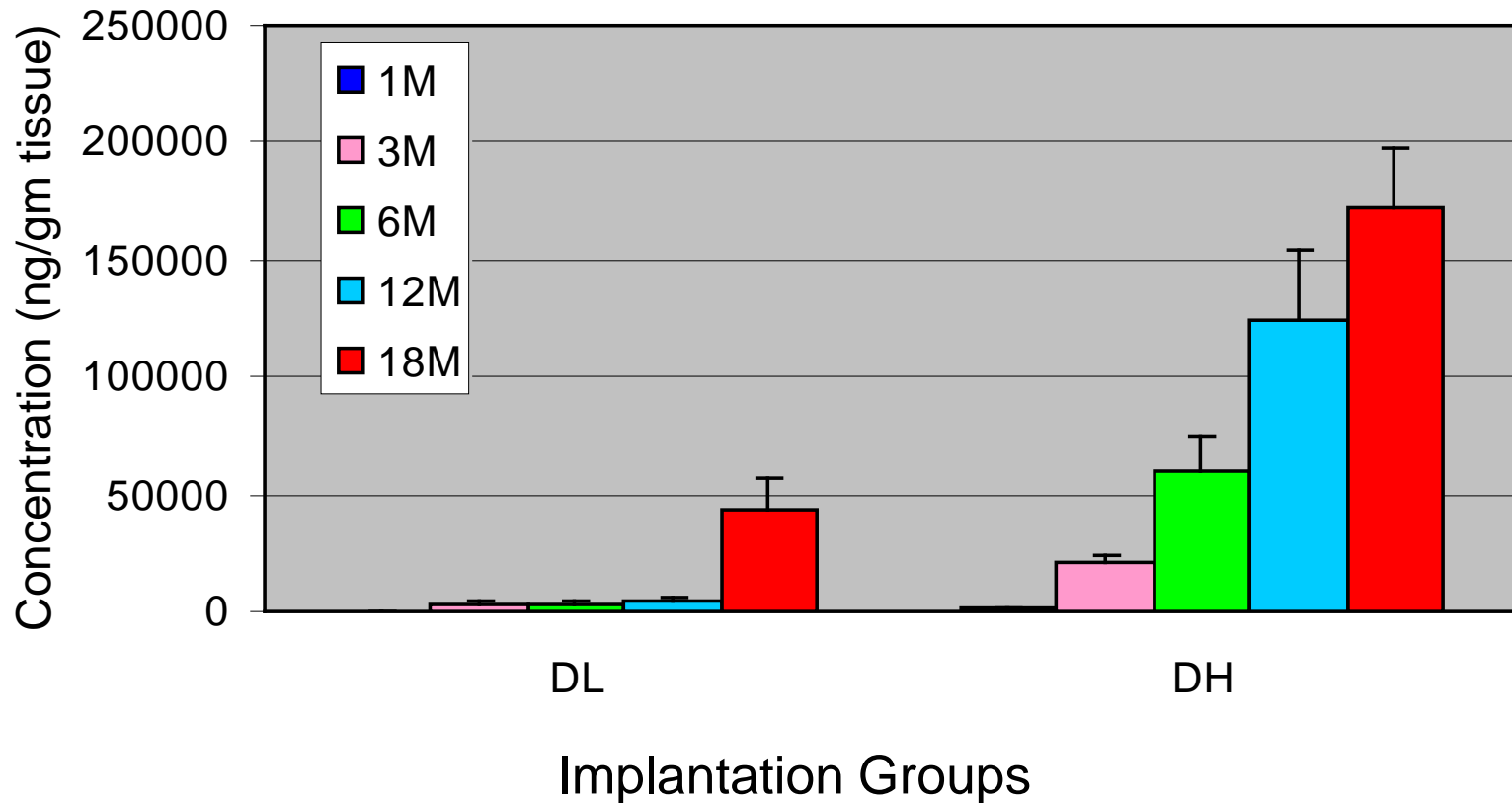
Fibrotic Capsule from DU Implantation Site (13 weeks)



DU Implantation Site – 13 weeks



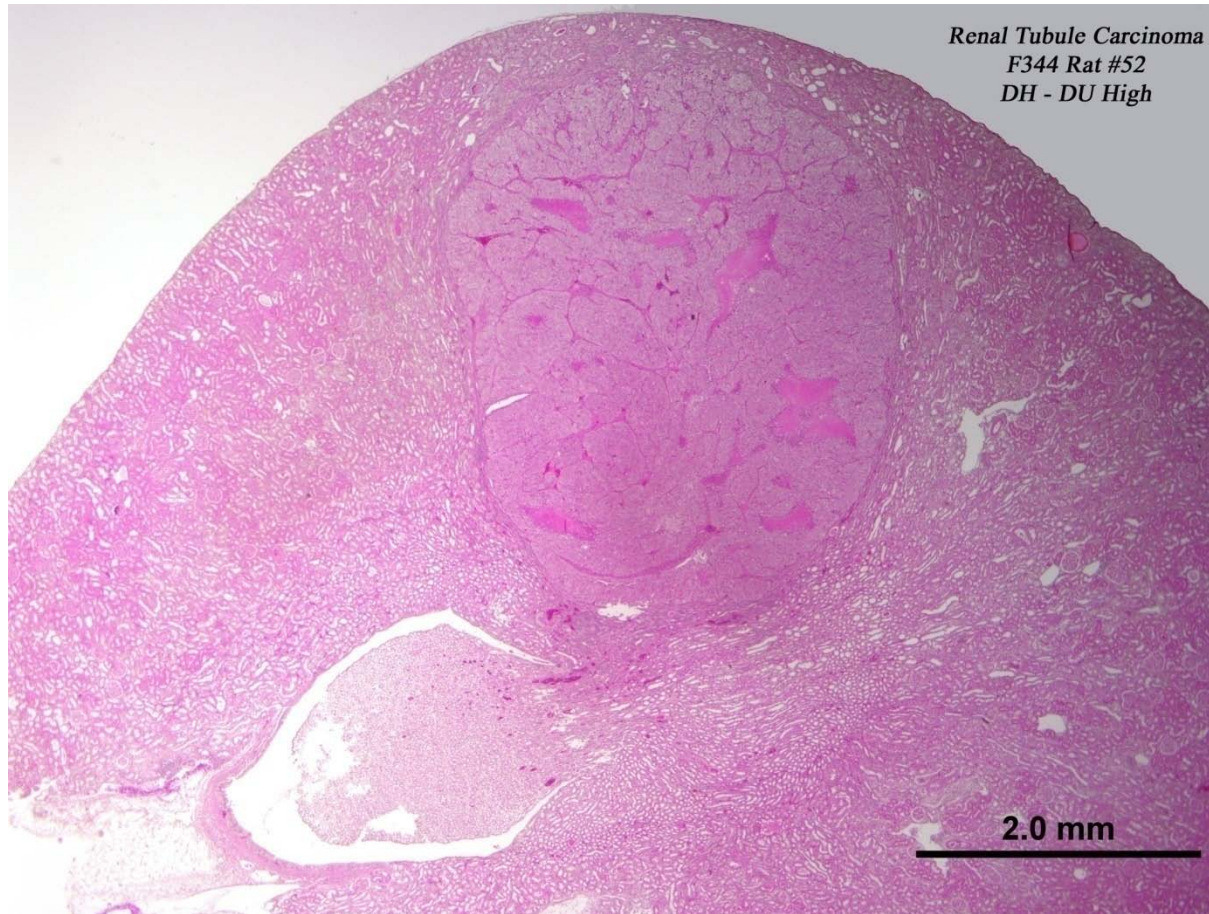
Popliteal Lymph Node Uranium Levels



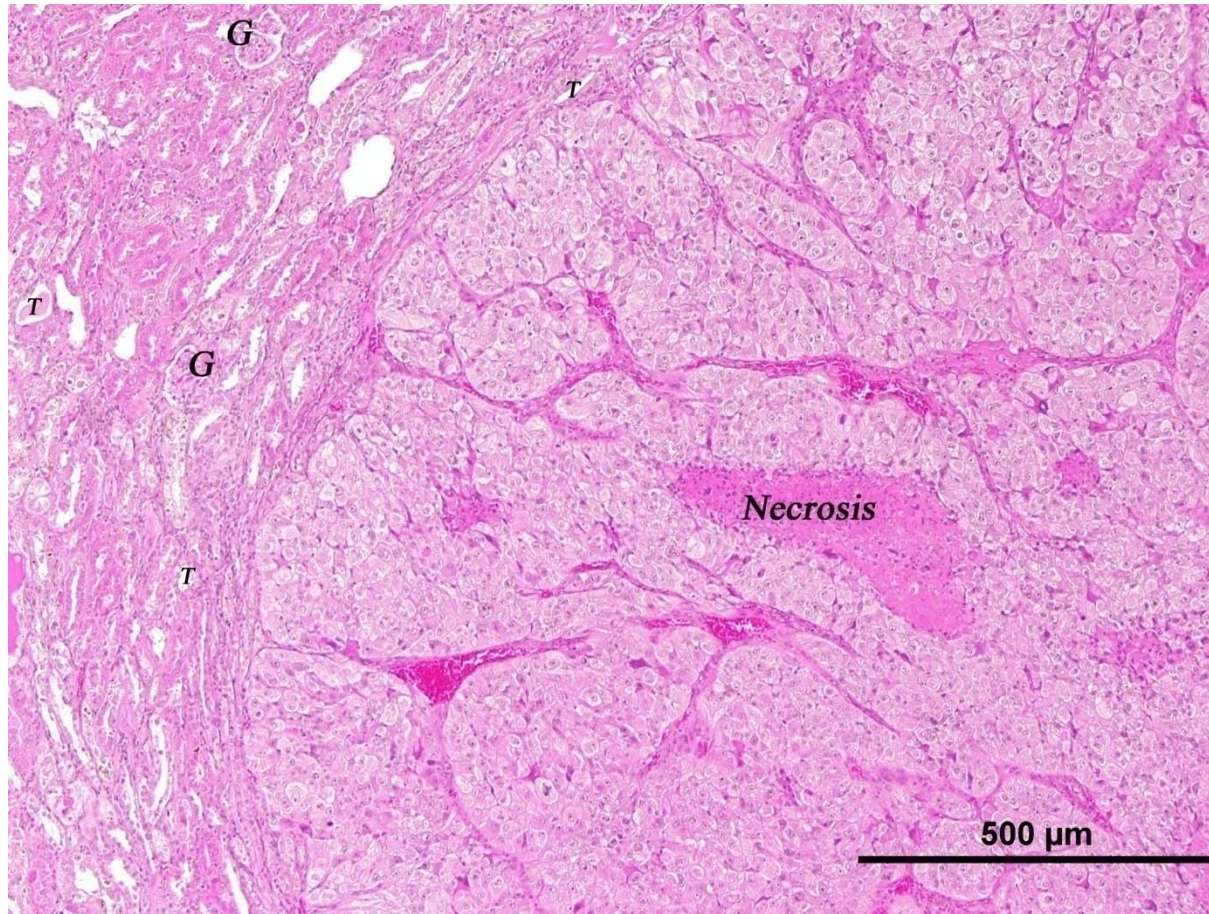
Tumor Distribution Based on Gross Necropsy Examination

	6 Month (n = 20)	12 Month (n = 20)	18 Month (n = 10)	24 Month (n = 16)
Non-surgical	None	1-abdominal	8-testicle	7-testicle 3-abdominal
Tantalum	2-abdominal	None	8-testicle 2-abdominal	9-testicle 5-abdominal 1-muscle (leg)
DU Low Dose	None	2-abdominal	8-testicle 1-abdominal	10-testicle 1-abdominal 1-adrenal 1-kidney
DU High Dose	None	2-abdominal 1-lung	6-testicle 2-abdominal 1-kidney	9-testicle 2-lung 8-kidney 1-muscle (leg)

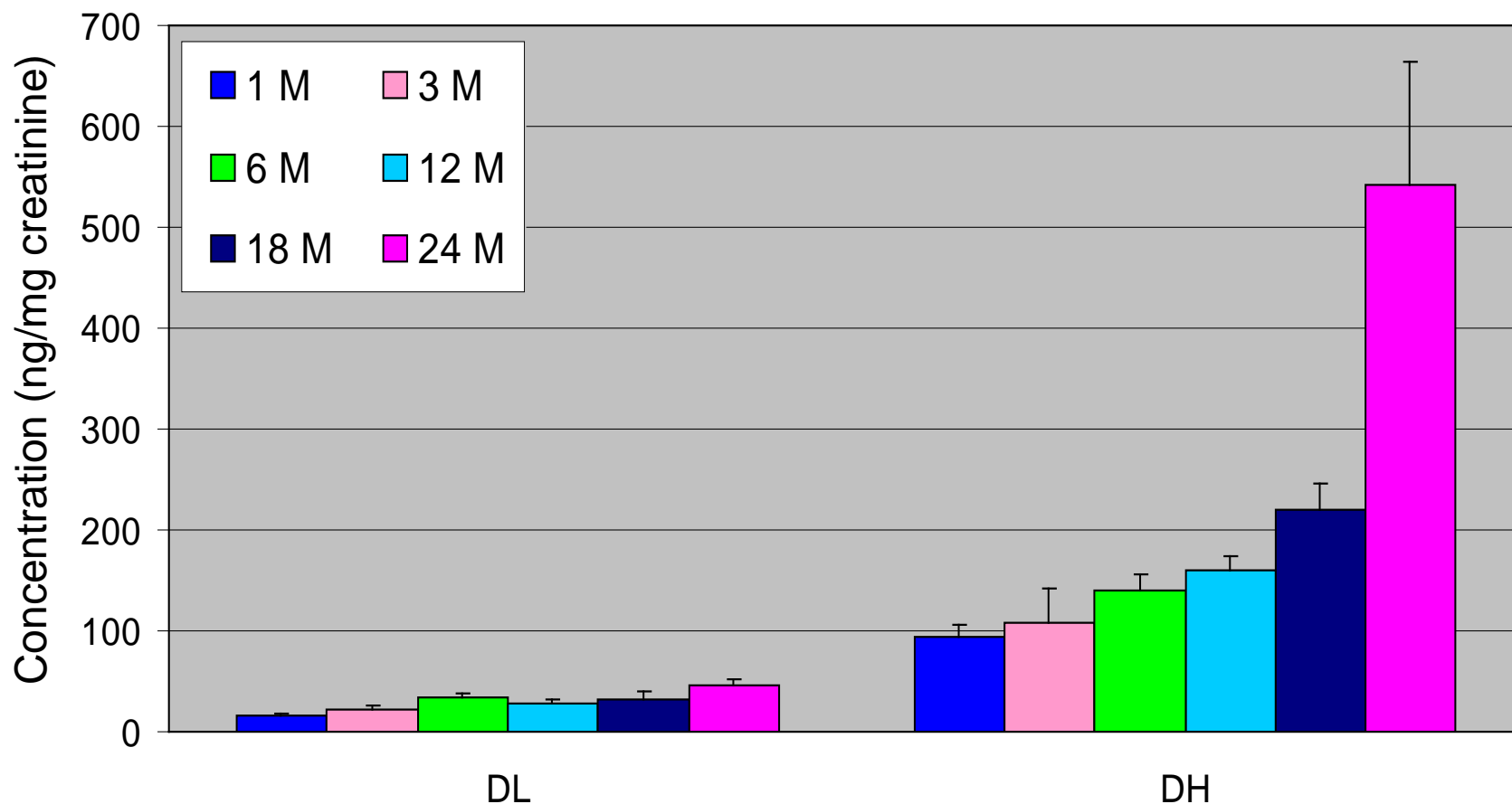
Renal Tubule Carcinoma – High-Dose DU (104 weeks)



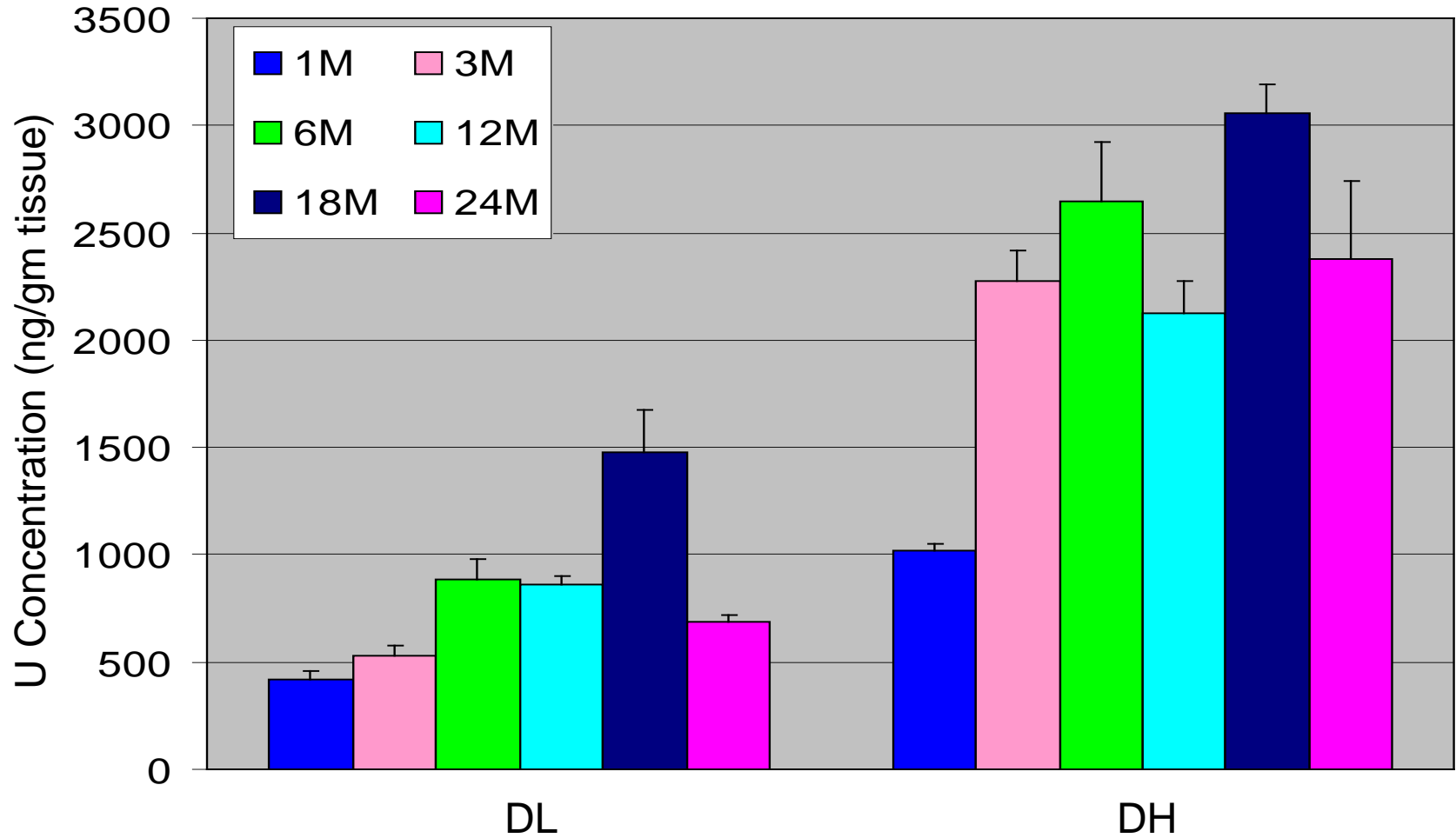
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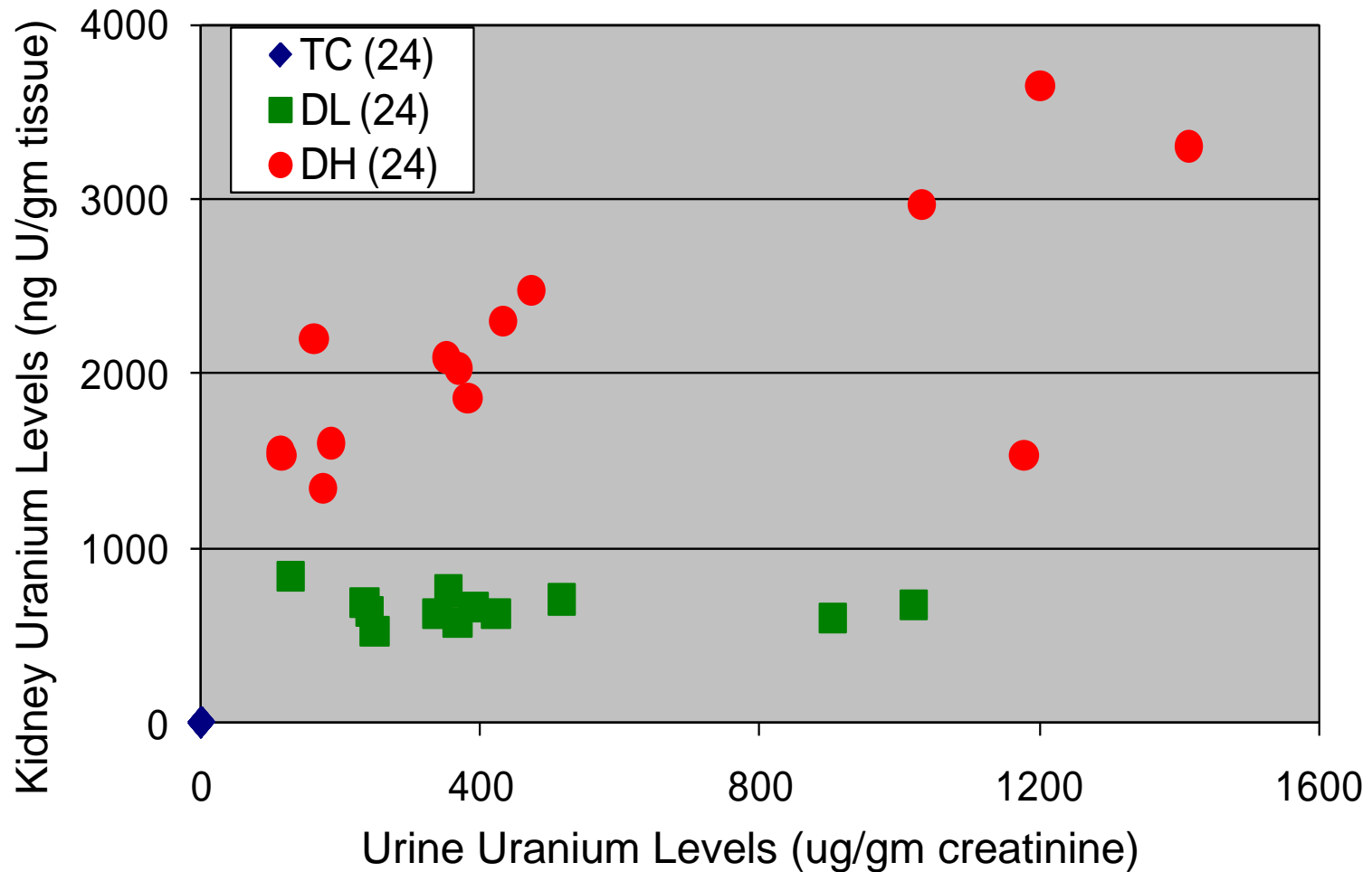
Urine Uranium Levels



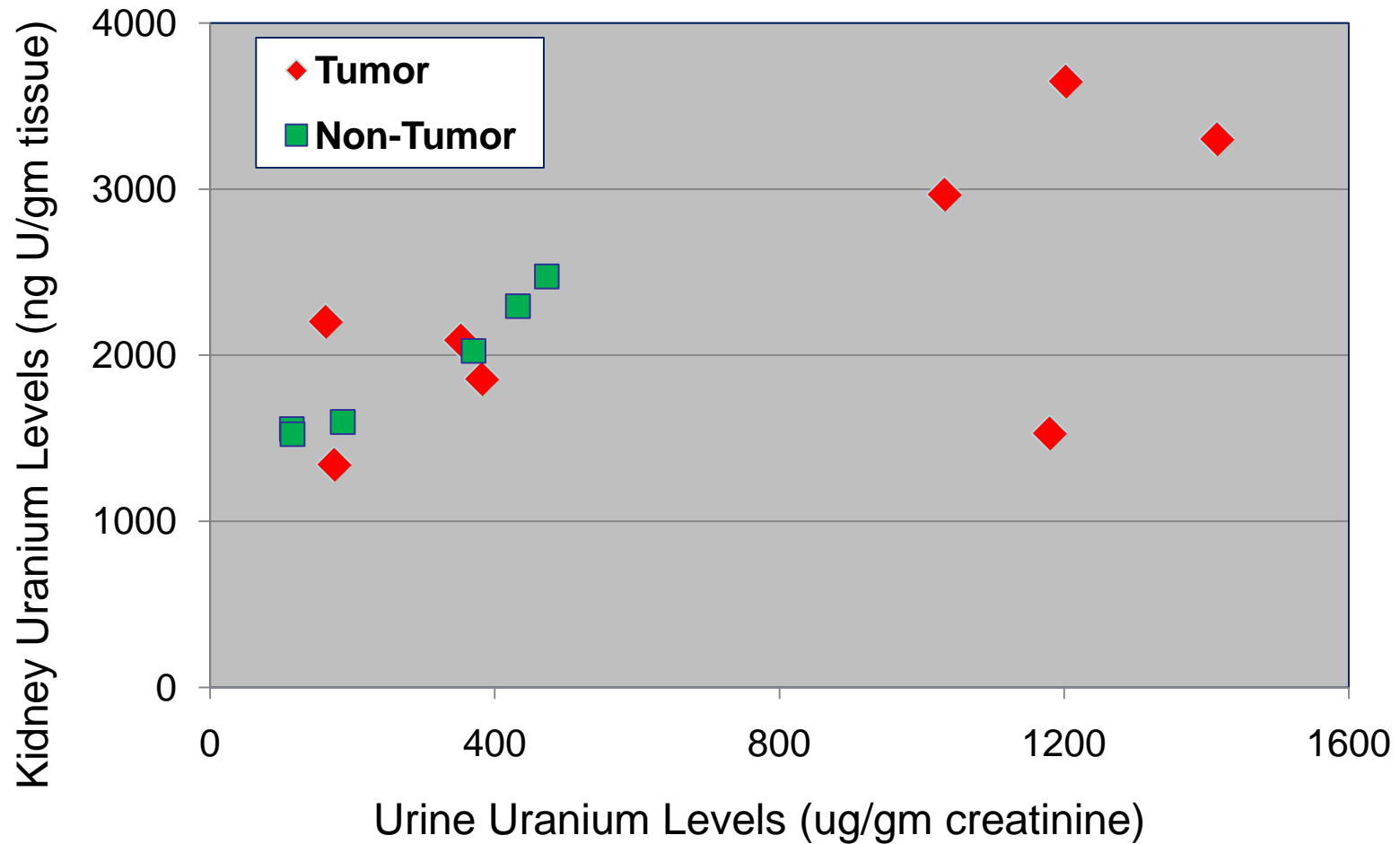
Kidney Uranium Levels



Correlation of Kidney and Urinary Uranium Levels



Uranium Levels in Rats with and without Renal Tumors



Summary

- DU-implanted rats did not exhibit tumors at the pellet implantation sites.
- High-dose DU rats, in the 24 month group, had an increased incidence of renal neoplasias.
- Urine uranium levels in DU-implanted rats increased over time in a dose-dependent manner.
- Uranium levels in the kidney also increased over time, reaching 3 $\mu\text{g/g}$ tissue by 18 months in the high-dose DU group.

Current Work

- Continue histopathology assessment of renal carcinomas

Future Directions

- Identify early serum or urinary biomarkers of DU-induced neoplastic renal changes
- Investigate molecular mechanisms associated with DU-induced renal effects
- Tier-testing approach for assessing potential health effects of embedded metal fragments

The “Team”

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QUESTIONS

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